UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,468	11/27/2006	Paolo Morazzoni	2503-1225	5191

466 7590 08/19/2010

YOUNG & THOMPSON
209 Madison Street
Suite 500
Alexandria, VA 22314

EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
08/19/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,468	MORAZZONI ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-46* is/are pending in the application.

4a) Of the above claim(s) *43045* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/27/2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the Appeal Brief filed on 5/27/2010 and 7/1/2010, PROSECUTION IS HEREBY REOPENED. The new 112, 1st enable rejection, 112, 2nd rejection, and103 rejections under Physiologics in view of Bombardelli, or further in view of Kim et al/Loew are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Terry A. McKelvey/

Supervisory Patent Examiner, Art Unit 1655

Claims 1-22 are cancelled. Claims 23-46 are pending. Claims 43-45 are withdrawn.

Claims 23-42 and 46 are examined on the merits.

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejection 112, 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-42 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a disease related with the reduction of cognitive function and mental fatigue, does not reasonably provide enablement for preventing a disease related with the reduction of cognitive function and mental fatigue, or preventing deterioration of the speed of memory in people with decreased cognitive function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the relative skill of those in the art; (5) the predictability or unpredictability of the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention is drawn to a method for treating and preventing a disease related with the reduction of cognitive function and mental fatigue, or a method for the enhancement of cognitive function and alleviation of mental fatigue by preventing deterioration of the speed of memory in people with decreased cognitive function.

Aging is a gradual, continuous process of spontaneous change that begins at birth and continues throughout all stages of life. With advanced age, a decline in mental function is nearly universal and is considered normal aging. This decline includes increased difficulty learning new languages and increased forgetfulness. In contrast, the decline that occurs in dementia is much more severe. For example, people who are aging normally may misplace things or forget details, but people who have dementia may forget entire events. People with dementia also have difficulty doing normal daily tasks (such as driving, cooking, and handling finances) and understanding the environment, including knowing what year it is and where they are. Thus, dementia is considered a disorder, even though it is common in late life (see Delirium and Dementia). Certain kinds of dementia, such as Alzheimer's disease, differ from normal aging in other ways as well. For example, brain tissue (obtained during autopsy) in people with Alzheimer's disease looks different from that in older people without the disease. So the distinction between normal aging and dementia is clear (see Introduction of aging from Merck Manuals, accessed on 7/28/2010, pp. 1-3).

(2) the breadth of the claims:

The Merck manual indicates that Dementia is a slow, progressive decline in mental function including memory, thinking, judgment, and the ability to learn. Alzheimer's disease is a progressive loss of mental function, characterized by degeneration of brain tissue, including loss of nerve cells and the development of senile plaques and neurofibrillary tangles (see Introduction of Dementia and Alzheimer's disease from Merck Manual, accessed on 7/28/2010, pp. 1-18).

Thus, the breadth of the claims encompasses by administering to a subject the claimed composition, the incidence of dementia or Alzheimer's disease is reduced to zero.

(3) the state of the art:

The claims imply that by taking the claimed composition, one will not have reduction of cognitive function and mental fatigue. This is contrasted by the finding of the prior art.

Jiao et al (Jiao et al, Metal-amyloid-.beta. peptide interactions: a preliminary investigation of molecular mechanisms for Alzheimer's disease, Science in China, Series B: Chemistry (2007), 50(4), 453-467) teach although humans have spent exactly 100 years combating Alzheimer's disease (AD), the molecular mechanisms of AD remain unclear. Owing to the rapid growth of the oldest age groups of the population and the continuous increase of the incidence of AD, it has become one of the crucial problems to modern sciences. It would be impossible to prevent or reverse AD at the root without elucidating its molecular Mechanisms (see Abstract).

Bacskai et al (Bacskai et al, Four-dimensional multiphoton imaging of brain entry, amyloid binding, and clearance of an amyloid-beta ligand in transgenic mice, Proceedings of the National

Academy of Sciences of the United States of America, (2003 Oct 14) Vol. 100, No. 21, pp. 12462-7) teach the lack of a specific biomarker makes preclinical diagnosis of Alzheimer's disease (AD) impossible, and it precludes assessment of therapies aimed at preventing or reversing the course of the disease).

Lee (Lee, Treatment of vascular dementia: a comprehensive review, Taehan Sin'gyong Kwahak Hoechi (2003), 21(5), 445-454) teaches vascular dementia is the second most common cause of dementia in the elderly after Alzheimer's disease. At present, there are only very limited data that might support either the prevention or the treatment of vascular dementia, despite a long history of attempts. Heterogeneity of vascular dementia complicated the study of treatment and its diagnostic paradigm based on Alzheimer's disease made it impossible to identify cases early enough to prevent the development of dementia (see Abstract).

Therefore, preventing reduction of cognitive function and mental fatigue is currently not attainable.

(4) the relative skill of those in the art

The relative skill in the art is high. The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g.M.D., Ph.D., Pharm. D. or combinations thereof).

(5) The predictability or unpredictability of the art:

Ashe et al (Ashe et al, Molecular basis of memory loss in the Tg2576 mouse model of Alzheimer's disease, Journal of Alzheimer's disease: JAD, (2006) Vol. 9, No. 3 Suppl, pp. 123-6) teach understanding the pathophysiology and treatment of Alzheimer's disease is vitally

important. Alzheimer's disease threatens to affect currently at least 30% of all individuals currently alive in the 12 most financially developed countries, unless interventions are discovered to prevent or treat the disease. Although memory loss is the cardinal symptom of Alzheimer's disease, the pathophysiological mechanisms leading to cognitive deficits are poorly understood. It is difficult to address this problem in human studies, and impossible in cultured cells. Therefore, animal models are needed to elucidate the molecular mechanisms leading to dementia. A large number of animal models have focused upon the role of amyloid plaques in the pathogenesis of Alzheimer's disease, because amyloid plaques are an essential diagnostic feature of the disease. However, the mechanism by which amyloid plaques or their principal molecular constituent, the amyloid-beta protein (Abeta), disrupt cognitive function is not well understood (see Abstract).

Dorner (Dorner, THE PSYCHO PATHOLOGY OF PRE SENILE DEMENTIAS A SURVEY, Aktuelle Neurologie, (1980) Vol. 7, No. 2, pp. 63-73) teaches the concept of presenile dementia is too narrow and restrictive, but it has not been replaced to date by any other equivalent expression, and hence is still in use. Practically any group of diseases can provoke presenile dementia. For reasons of preventive medical care, it is considered important to achieve broad-spectrum sensitization on the problem of progressive functional failure of the brain, and large-scale screening is urged. Disease patterns of affective disorders or of schizophrenia will frequently render proper differential diagnosis difficult. Wrong diagnoses in this respect are stated to be of the order of about 30%, as communciated by a catamnestic study. Greatest diagnostic prudence is mandatory in any disease pattern which appears contradictory from a psychopathological point of view, and which does not present a uniform pattern or seems

improbable or even impossible. Besides treating genuine or false presenile dementias in a suitable manner, and their early identification, the social framework surrounding these presenile dementias with unfavorable prognosis must not be neglected. It seems that eugenic guidance of families in whom Huntington's chorea runs on a hereditary basis, has remained an unsolved problem to date which merits closer attention (see Abstract).

Therefore, preventing a disease related with the reduction of cognitive function and mental fatigue is unpredictability in the art

(6) The amount of direction or guidance presented.

The specification has not provided guidance on prevention of reduction of cognitive function and mental fatigue by using the claimed composition.

(7) The presence or absence of working examples.

There is no working example regarding how to prevent reduction of cognitive function and mental fatigue by using the claimed composition.

(8) The quantity of experimentation necessary:

Since preventing a disease related with the reduction of cognitive function and mental fatigue is such a complex issue, the state of the art has not been able to prevent a disease related with the reduction of cognitive function and mental fatigue from happening. Plus the claimed composition has not able to reduce the incidence of reduction of cognitive function and mental fatigue to zero, and the specification has not provided any guidance regarding how to prevent reduction of cognitive function and mental fatigue using the claimed composition, the quantity of experimentation is undue. Further more, in order to prevent reduction of cognitive function and

mental fatigue, the treatment regimen must be identified, and the end point of the prevention also needs to be identified. Since the Applicant have not provided the appropriate time frame and dosage at which the composition should be administered to prevent reduction of cognitive function and mental fatigue, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the claimed composition would be effective in preventing reduction of cognitive function and mental fatigue.

Based on the aforementioned reasons the Examiner concludes that the specification, while being enabling for treating a disease related with the reduction of cognitive function and mental fatigue, does not reasonably provide enablement for preventing a disease related with the reduction of cognitive function and mental fatigue, or preventing deterioration of the speed of memory in people with decreased cognitive function. Since the state of the art is highly unpredictable and requires much greater guidance for an ordinary skilled artisan to effectively prevent a disease related with the reduction of cognitive function and mental fatigue, or prevent deterioration of the speed of memory in people with decreased cognitive function, burdensome experimentation, such as clinical studies would necessarily be required of the ordinary skilled artisan to establish the prevention of a disease related with the reduction of cognitive function and mental fatigue.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recites "at least about 20%" in line 2. The term "at least about 20%" in claim 28 is a relative term which renders the claim indefinite. The term "at least about 20%"" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. At the surface, "at least about 20%" could be construed as more than 20%. However, 17% is "about 20%", therefore 18% could be considered as "at least about 20%".

Therefore, the metes and bounds of claims are rendered vague and indefinite. The lack of clarity renders the claims very confusing and ambiguous since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-26, 29-40, and 46 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics (Physiologics, Physphatidylserine complex with Ginkgo, 2003,

online document provided as IDS by Applicant on 7/27/2006), in view of Bombardelli (EPA 0275005) (provided as IDS by Applicant on 7/27/2006).

Physiologics teaches dietary supplement of 60 softgels (thus in the form of capsules/gels, thus the limitation of claim 30 is met, thus for oral administration, thus the limitation of claim 31 is met). Physiologics teaches phosphatidylserine complex with Ginkgo biloba is perfect for mild memory problems associated with aging (thus a method for the enhancement of cognitive function and alleviation of mental fatigue by improving the speed of memory and memory quality, by counteracting cognitive fatigue in normal and healthy persons, thus a method for the treatment of a disease related with the reduction of cognitive function, such as dementia or Alzheimer's disease). Physiologics teaches phosphatidylserine plays a role in neurotransmissions and supports cognitive function while Ginkgo biloba helps improve memory (col 1, 1st paragraph). Physiologics teaches phospholipid complex from soy lecithin standardized to contain 20% phosphatidylserine, 100 mg (thus a phospholipid containing 10-50%, 20-40%, or 20% of phosphatidylserine, thus the limitations of claims 23-25 are met). Physiologics teaches the product containing Ginkgo biloba extract 30 mg (standardized to contain 24% Ginkgo flavone glycosides) (thus at least 20% Ginkgo flavone) (3rd column, Supplement Facts). Thus the ratio between Ginkgo and the phosphatidylserine is about 1:3 (thus the limitations of claims 29 and 46 are met). Physiologics also teaches the product comprising 5 mg vitamin C (3rd column, Supplement Facts) (thus a pharmaceutically acceptable amount of at least one additive selected from vitamins, thus the limitation of claims 33 and 34 are met).

Physiologics does not teach forming a complex between Ginkgo and phosphatidylserine; neither does Physiologics teach the claimed dosage in claim 32.

Bombardelli teaches complex compounds of flavonoids with phospholipids, characterized by high lipophilia and improved bioavailability and therapeutic properties as compared with free, not complexed flavonoids. The complex compounds of the invention are suitable for use as the active principle in pharmaceutical and cosmetic (see Abstract). Bombardelli also teaches complex compounds of flavonoids with phospholipids (claim 1), wherein the phospholipids are selected from phosphatidyl serine, etc (claim 4), and wherein the flavonoids are selected from the group consisting of ginkgonetine, isoginkgonetine and bilobetine (claim 5), etc (thus Ginkgo biloba extract). Bombardelli also teaches the invention also provides a process for purifying flavonoids form plants such for example as Ginkgo biloba etc (page 3, 6th paragraph). Bombardelli further teaches the preparation of ginkgo biloba depurated extract /total soy phospholipids complex (page 10, Example 11).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to form a complex of Ginkgo biloba extract with phosphatidylserine in Physiologics since Bombardelli teaches complex of flavonoids and phospholipids has high lipophilia and it improves bioavailability; Bombardelli also teaches the preparation of ginkgo biloba extract and soy phospholipids complex as an example. Therefore, it would have been obvious for one of the ordinary skill in the art to form complex of Ginkgo biloba extract with soy phospholipid containing 20% phosphatidylserine in Physiologics to improve bioavailability so as to enhance cognitive function and alleviate of mental fatigue.

Regarding the limitation to the claimed dosage in claim 32, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. It has been held that where

the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. The differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). see MPEP § 2144.05 part II A. Although the prior art did not specifically disclose the claimed dosage in claim 32, it would have been obvious to

one of ordinary skill in the art at the time Applicants' invention was made to determine the dosage of phosphatidylserine complex with Ginkgo biloba because the amount of the claimed components is art-recognized result effective variables because it has the ability enhance memory function, which would have been routinely determined and optimized in the pharmaceutical art.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 23-41, and 46 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics and Bombardelli as applied to claims 23-26, 29-40, and 46 above, and further in view of Loew (Value of Ginkgo biloba in treatment of Alzheimer dementia, Wiener medizinische Wochenschrift (1946), (2002) Vol. 152, No. 15-16, pp. 418-22. Ref: 40).

The teachings of Physiologics and Bombardelli are set forth above and applied as before.

The combination of Physiologics and Bombardelli do not specifically teach the principle active substance of Ginkgo biloba extract is bilobalide, the Ginkgo extract contains 2-10% terpene lactones, or the incorporation of acetylcholinesterase inhibitor into the composition.

Loew teaches Ginkgo biloba special extract Egb 761 is a standardized and highly purified extract of Ginkgo leaves. Among the active constituents are the ginkgo-flavone glycosides and the terpene-lactones (ginkgolides, bilobalide). The presence of these constituents in Ginkgo extracts, which constituents are known to be useful for treating Alzheimer's disease, provides the

rationale for clinical trials in vascular dementia and primary degenerative dementia of the Alzheimer's disease, and in mixed forms of both. In clinical trials of different working-groups, effects of Ginkgo biloba on the cognitive performance, global function, and activities of the daily living have been found. Metaanalysis in the indication—demential disorders--comparing Ginkgo biloba versus acetylcholinesterase inhibitors have shown a similar clinical efficacy of both therapy regimens with an additional drug safety benefit for Ginkgo. Loew further teaches that clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the ginkgo-flavone glycosides and 2-10% terpene-lactones (ginkgolides, bilobalide) from Loew in the enhancement of cognitive function as Loew explicitly teaches Ginkgo biloba extract contains those components. It would have been *prima facie* obvious for one of ordinary skill in the art to include acetylcholinesterase inhibitors in the composition since Loew teaches Ginkgo biloba has shown a similar clinical efficacy with acetylcholinesterase inhibitors, and clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 23-26, 29-40, 42, and 46 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Physiologics and Bombardelli as applied to claims 23-26, 29-40, and 46 above, and further in view of Kim et al (Kim et al, Proteomics of neuroprotective actions of grape seed extract, FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp).

The teachings of Physiologics and Bombardelli are set forth above and applied as before.

The combination of Physiologics and Bombardelli do not specifically teach the incorporation of grape seed extract into the composition.

Kim et al teach certain botanicals are purported to have health benefits because of anti-oxidant activity intrinsic to their polyphenol content. Grape seed extract (GSE) preparations, enriched in the proanthocyanidins, are in this category. Animal behavior studies showed that dietary supplementation with blueberry extract, enriched in proanthocyanidins similar to those in GSE, protected against age-related cognitive decline (see Abstract).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to incorporate the grape seed extract from Kim et al into the composition of Physiologics since Kim et al teach Grape seed extract (GSE) preparations, enriched in the proanthocyanidins, protected against age-related cognitive decline. Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to incorporate the grape seed extract from Kim et al into the composition of Physiologics for the enhancement of cognitive function.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Examiner, Art Unit 1655